

# COOK®

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## Cook Group Incorporated

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August 13, 2004

Ms. Joanne Less  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, Maryland 13852

Re: Docket No. 2004-N-0254

Dear Ms. Less:

This comment is filed on behalf of the Cook Group, Inc. ("Cook"), a holding company of international corporations engaged in the manufacture of diagnostic and interventional products for radiology, cardiology, urology, gynecology, gastroenterology, wound care, emergency medicine, and surgery. Cook pioneered the development of products used in the Seldinger technique of angiography, and in techniques for interventional radiology and cardiology. Cook products benefit patients by providing doctors with a means of diagnosis and intervention using minimally invasive techniques, as well as by providing innovative products for surgical applications. Cook sells over 15,000 different products which can be purchased in over 60,000 combinations. Many of these devices are used by physicians in the care and treatment of children.

We are writing in response to the request from the Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), for comments concerning possible barriers to the availability of medical devices intended to treat children. As mentioned above, Cook manufactures and markets many products for children, and we believe our nation should be firmly committed to providing children with the highest quality and most current medical technology. There are barriers to fully serving pediatric markets, however, and we are gratified to have the opportunity to share our views of those barriers with FDA and to make suggestions for overcoming them.

At the outset, we should not be confused about the types of devices we need to address in these comments. The safety and effectiveness of most devices is immediately known for children as well as adults. There is a smaller group of devices, however, that may have long term effects upon pediatric populations. With respect to these types of devices, we make the following observations:

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- The principal difficulty in serving pediatric markets arises from the small number of children that are affected by most conditions. It certainly is a good thing that relatively few children face serious medical problems. However, it is difficult, if not impossible, to enlist a significant number of pediatric patients in a clinical trial with a novel product, because so few patients are available, and those that are available are scattered across the country.
- Because the demand for pediatric devices is so small, and the cost of developing pediatric devices is so large, manufacturers are reluctant to develop them or to label medical devices for pediatric indications.
- The pediatric population is constantly changing. Today's pediatric patient is tomorrow's adult. Artificial limbs, for example, which may be appropriate at one stage of pediatric development, may be wholly inappropriate at a later stage.
- Materials which are biocompatible with adults are generally biocompatible with children, but, in a few instances, are not.
- Growth factors, extent of psychosocial development, and the difficulty in obtaining informed consent from the patient are just several of the additional factors which compound the difficulty of conducting clinical trials in pediatric populations.

Due to the unique characteristics of the pediatric population, we believe that it is important that the government take steps to improve access to pediatric products, and we offer the following suggestions for your consideration.

#### **1. Humanitarian Device Exemption (HDE)**

The humanitarian device exemption was enacted by Congress to encourage the development of products to treat or diagnose conditions which affect small patient populations of less than 4,000 patients per year. The concept of the HDE is to reduce the regulatory burdens and costs for sponsors of orphan products in recognition of the fact that such products will not generate significant revenues. It should be emphasized that the provision **reduces** regulatory barriers. It does not eliminate them. There are a number of requirements which must be met by sponsors before a product is approved to assure protection of the public health. Unfortunately, in addition to these requirements, sponsors are prohibited from making profits on products which have been awarded an HDE.

Since enactment of the HDE provision in 1990, there have been only thirty-four HDE's approved by FDA. The fetal bladder stent manufactured by Cook was the first HDE granted by FDA. Some of these products, like the fetal bladder stent, have been life saving. None of these products would have come to market without the

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HDE because of the difficulties associated with populating clinical trials or the heavy financial burdens of such trials.

We believe that many more products would have reached patients through the humanitarian device exemption, had not the prohibition on profits been included in the law. We have consistently advocated that this prohibition be eliminated. As it focuses on the needs of children, we urge FDA to recommend to Congress that the prohibition be removed, at least for the pediatric population. The key in these small marketplaces is to reduce costs and increase incentives for manufacturers wherever possible. The humanitarian device exemption has provided a way to reduce costs. Economic incentives provided by the opportunity for profit should be allowed to work freely. In our opinion, this will encourage manufacturers to address pediatric needs. Many manufacturers will readily enter markets of only a few thousand per year if there is a streamlined regulatory process and the ability of the marketplace to generate a profit, present everywhere else in our healthcare system, is unfettered.

We also recommend that the requirement for IRB approval for each individual use of a device approved under the HDE should be significantly modified or excluded. This requirement has created confusion among institutions and added to the burdens of those trying to provide these products through the exemption.

Finally, we suggest that the threshold number of patients necessary to qualify for a humanitarian devices exemption should be re-examined. The current threshold of 4,000 patients was arrived at arbitrarily, and we believe it is unduly restrictive. The "orphan" market for drugs is defined at 130,000 patients per year, and while we do not have data demonstrating the appropriate market for devices, we believe the appropriate threshold for medical devices should be significantly higher than it is currently. To reiterate once more, there are safeguards within the HDE statutory framework to ensure safety and ensure inappropriate use. These safeguards would not be mitigated by establishing a higher threshold population.

## **2. Pediatric Device Research Network**

There are many institutions across the United States, that are dedicated, at least in part, to treating diseases and conditions that affect children. Establishing a network of institutions that could assist sponsors of medical technology in recruiting patients for clinical trials during the approval process, would be very helpful to those manufacturers who seek to address the needs of pediatric populations. This network could also be helpful with data coordination and publication of peer-reviewed data.

### **3. Grants**

There are a number of programs within FDA and NIH to assist those who are developing products for a small patient population. We recommend that as part of its report, FDA identify which programs could be most useful in encouraging the development of pediatric products, and suggest new programs to Congress if those currently existing are not sufficient. Grants can reduce the costs of those who wish to develop products for children, and, if they are large enough, there are enough of them, and their existence is well known, they will assist in the goal of developing more pediatric products.

### **4. Historical Data**

We believe that historical data is always valuable in the approval process and should be utilized wherever possible, particularly in pediatric populations where the number of patients is so small and controls are difficult to establish. In these circumstances, historical data can and should be used to compensate for the complexities of collecting clinical trial data given the underlying reality of a small patient population.

### **5. Use Of Information**

Many medical technologies are used today for off-label purposes, particularly in treating small patient populations. Physicians often collect significant data regarding the safety and effectiveness of off-label uses. Unfortunately, the law constrains FDA in considering data gained from off-label use in product approval applications. We recommend that FDA undertake a legal analysis of these constraints to determine if they can be removed. To the extent that a statutory change is required, we recommend that FDA propose legislation to Congress to permit the utilization of such data with appropriate safeguards to ensure against abuse by manufacturers. Utilizing such data can significantly expedite the approval of new conditions of use for important technologies, particularly for small patient populations.

Further, current law prohibits FDA from sharing information it has gained from other applications. We believe that there is a strong case for major long-term reform regarding the use of information. In the short term, we recommend that steps be taken to permit FDA to share information regarding any issues which arise involving biocompatibility of materials for pediatric products. The public needs to be alerted to both problems and solutions.

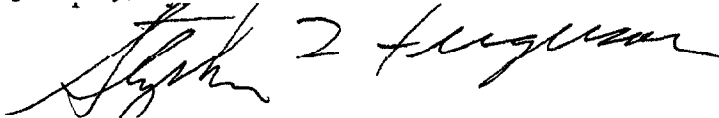
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Several of the changes we have recommended will require legislative action. Congress will need to amend the provisions of the Federal Food, Drug, and Cosmetics Act governing the humanitarian device exemption and perhaps improve programs offering grants. It will also need to provide funding at appropriate levels for these programs. It will probably be necessary to make statutory changes to establish a pediatric network and to broaden the use of information as well. We respectfully urge FDA to recommend such changes in its report to Congress later this year.

We are very grateful for the opportunity to offer our thoughts on this very important subject, and we commend the agency for making the significant effort to analyze issues affecting children and medical technology. America's children truly are its future, and they deserve nothing but the finest medical care.

Thank you again for consideration of our comments.

Respectfully,

A handwritten signature in black ink, appearing to read "Stephen L. Ferguson". The signature is fluid and cursive, with the first name "Stephen" being more legible than the last name "Ferguson".

Stephen L. Ferguson